



STIC Search Report

EIC 3700

STIC Database Tracking Number: 146974

TO: Samuel Gilbert
Location: RND 7a25
Art Unit: 3736

3/18/05

Case Serial Number: 10/705989

From: Jeanne Horrigan
Location: RND 8A34
Phone: 571-272-3529

jeanne.horrigan@uspto.gov

Search Notes

Attached are the search results for the method of treating remodeling.

I tagged the references that I thought were most useful, but I suggest that you review ALL of the results.

Also attached is a search feedback form. Completion of the form is voluntary. Your completing this form would help us improve our search services.

I hope the attached information is useful. Please feel free to contact me if you have any questions or need additional searching on this application.

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Samuel Gilbert Examiner #: 70632 Date: 3/7/05
Art Unit: 3736 Phone Number 90 272-4725 Serial Number: 10/705 989
Mail Box and Bldg/Room Location: Rm 725 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Expandable Cardiac Harness for treating Congestive Heart Failure
Inventors (please provide full names): Lillip Lau ; Bill Hertigan

Earliest Priority Filing Date: 3/10/2000

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

method of stretching a heart (treating reverse remodeling)

- placing an elastic jacket (harness) on the heart

must X - providing elastic resistance to stretch during diastole and contractile augmentation during systole.

not needed in all methods - decreasing elastic resistance as reverse remodeling occurs

Received 3/7/05 11:15a J.S.

STAFF USE ONLY
Searcher: Jeanne Benigan
Searcher Phone #: 23529
Searcher Location: _____
Date Searcher Picked Up: 3/18/05
Date Completed: _____
Searcher Prep & Review Time: _____
Clerical Prep Time: _____
Online Time: _____

Type of Search	Vendors and cost where applicable
NA Sequence (#) _____	STN _____
AA Sequence (#) _____	Dialog _____
Structure (#) _____	Questel/Orbit _____
Bibliographic _____	Dr.Link _____
Litigation _____	Lexis/Nexis _____
Fulltext _____	Sequence Systems _____
Patent Family _____	WWW/Internet _____
Other _____	Other (specify) _____



STIC Search Results Feedback Form

EIC 3700

Questions about the scope or the results of the search? Contact **the EIC searcher or contact:**

John Sims, EIC 3700 Team Leader
RND 8B35, Phone 2-3507

Voluntary Results Feedback Form

➤ I am an examiner in Workgroup: Example: 3730

➤ Relevant prior art **found**, search results used as follows:

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☐ Helped examiner better understand the invention.
- ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
(journal articles, conference proceedings, new product announcements etc.)

➤ Relevant prior art **not found**:

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC/EIC3700 RND 8B31



File 149:TGG Health&Wellness DB(SM) 1976-2005/Mar W1
 (c) 2005 The Gale Group
 File 16:Gale Group PROMT(R) 1990-2005/Mar 18
 (c) 2005 The Gale Group
 File 160:Gale Group PROMT(R) 1972-1989
 (c) 1999 The Gale Group
 File 148:Gale Group Trade & Industry DB 1976-2005/Mar 18
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 File 369:New Scientist 1994-2005/Mar W1
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 File 370:Science 1996-1999/Jul W3
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 File 636:Gale Group Newsletter DB(TM) 1987-2005/Mar 18
 (c) 2005 The Gale Group
 File 441:ESPICOM Pharm&Med DEVICE NEWS 2005/Feb W2
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Set	Items	Description
S1	63106	REMODELING
S2	3084916	REVERS??? OR TREAT? OR PREVENT?
S3	600532	HEART OR CARDIAC()APEX OR VENTRICLE OR VENTRICULAR OR PERI-CARDI? OR EPICARDI?
S4	12176	DIASTOLE OR DIASTOLIC
S5	2963235	RESIST? OR LIMIT???
S6	3701568	STRETCH??? OR DISTENTION OR DISTENT??? OR STRAIN??? OR SWE-LL??? OR DIALT??? OR EXPAND??? OR EXPANSION
S7	8002	SHAPE(1N)CHANG???
S8	3540727	SYSTOLE OR SYSTOLIC OR CONTRACT???
S9	3666930	AUGMENT? OR AID??? OR ASSIST? OR FORCE
S10	174139	HARNESS OR HARNESES OR JACKET? ? OR SOCK? ? OR GIRDLE? ? - OR GIRDLING ORWRAP? ? OR SPLINT? ?
S11	570015	BIND??? OR BOUND OR CONSTRAINT? ?
S12	123878	GIRDLING OR WRAP? ?
S13	2204	DISTEND???
S14	134	S2(1W)S1
S15	27	S10:S12 AND S14
S16	22	(S4:S9 OR S13) AND S15
S17	19	RD (unique items)
S18	3	S17/2001
S19	2	S17/2002
S20	6	S17/2003
S21	1	S17/2004:2005
S22	7	S17 NOT S18:S21
S23	7	Sort S22/ALL/PD,A [not relevant]
S24	5	S15 NOT S16
S25	3	RD (unique items) [not relevant]
S26	30	S1(S)S3(S)S10:S12
S27	27	S26 NOT S15
S28	21	RD (unique items)
S29	3	S28/2001
S30	4	S28/2002
S31	1	S28/2003
S32	3	S28/2004:2005
S33	10	S28 NOT S29:S32
S34	10	Sort S33/ALL/PD,A [not relevant]

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S35 68073 S10/TI,DE OR S11/TI,DE OR S12/TI,DE
S36 1 S14 AND S35 [not relevant]

File 20:Dialog Global Reporter 1997-2005/Mar 18

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Set	Items	Description
S1	15725	REMODELING
S2	3190824	REVERS??? OR TREAT? OR PREVENT?
S3	819914	HEART OR CARDIAC()APEX OR VENTRICLE OR VENTRICULAR OR PERI-CARDI? OR EPICARDI?
S4	866	DIASTOLE OR DIASTOLIC
S5	2974893	RESIST? OR LIMIT???
S6	2693066	STRETCH??? OR DISTENTION OR DISTENT??? OR STRAIN??? OR SWE-LL??? OR DIALT??? OR EXPAND??? OR EXPANSION
S7	5647	SHAPE(1N)CHANG???
S8	3069233	SYSTOLE OR SYSTOLIC OR CONTRACT???
S9	4004079	AUGMENT? OR AID??? OR ASSIST? OR FORCE
S10	197942	HARNES OR HARNESSES OR JACKET? ?*OR SOCK? ? OR GIRDLE? ? - OR GIRDLING ORWRAP? ? OR SPLINT? ?
S11	532953	BIND??? OR BOUND OR CONSTRAINT? ?
S12	118465	GIRDLING OR WRAP? ?
S13	955	DISTEND???
S14	33	S2(1W)S1
S15	6	S10:S12 AND S14
S16	5	RD (unique items) [not relevant]
S17	27	S14 NOT S15
S18	24	RD (unique items)
S19	19	S18/2001:2005
S20	5	S18 NOT S19 [not relevant]

File 155:MEDLINE(R) 1951-2005/Mar W2

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File 5:Biosis Previews(R) 1969-2005/Mar W2

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File 73:EMBASE 1974-2005/Mar W2

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File 34:SciSearch(R) Cited Ref Sci 1990-2005/Mar W2

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File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec

(c) 1998 Inst for Sci Info

File 94:JICST-EPlus 1985-2005/Feb W1

(c)2005 Japan Science and Tech Corp(JST)

File 95:TEME-Technology & Management 1989-2005/Feb W1

(c) 2005 FIZ TECHNIK

File 99:Wilson Appl. Sci & Tech Abs 1983-2005/Feb

(c) 2005 The HW Wilson Co.

File 144:Pascal 1973-2005/Mar W1

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File 6:NTIS 1964-2005/Mar W1

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File 8:Ei Compendex(R) 1970-2005/Mar W1

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File 2:INSPEC 1969-2005/Mar W1

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File 35:Dissertation Abs Online 1861-2005/Feb

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Serial 10/705989

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File 65:Inside Conferences 1993-2005/Mar W2

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Set	Items	Description
S1	124575	REMODELING
S2	14843278	REVERS??? OR TREAT? OR PREVENT?
S3	3244407	HEART OR CARDIAC()APEX OR VENTRICLE OR VENTRICULAR OR PERI-CARDI? OR EPICARDI?
S4	252080	DIASTOLE OR DIASTOLIC
S5	7041231	RESIST? OR LIMIT???
S6	4375014	STRETCH??? OR DISTENTION OR DISTENT??? OR STRAIN??? OR SWE-LL??? OR DIALT??? OR EXPAND??? OR EXPANSION
S7	38710	SHAPE(1N)CHANG???
S8	1218962	SYSTOLE OR SYSTOLIC OR CONTRACT???
S9	4476340	AUGMENT? OR AID??? OR ASSIST? OR FORCE
S10	67360	HARNESS OR HARNESES OR JACKET? ? OR SOCK? ? OR GIRDLE? ? - OR GIRDLING ORWRAP? ? OR SPLINT? ?
S11	4769970	BIND??? OR BOUND OR CONSTRAINT? ?
S12	15765	DISTEND???
S13	17925	GIRDLING OR WRAP? ?
S14	1743	S2(1W)S1
S15	956740	ELASTIC?
S16	37	(S10 OR S13) AND S14
S17	110	S11 AND S14
S18	67	S16:S17 AND (S4 OR S8 OR S15)
S19	24	RD (unique items)
S20	12	S19/2001:2003
S21	4	S19/2004:2005
S22	8	S19 NOT S20:S21
S23	8	Sort S22/ALL/PY,A
S24	74116	S5(1W)S6:S7
S25	17	S5(1W)S12
S26	3235	8(1N)S9
S27	0	S S8(1N)S9
S28	28252	S8(1N)S9
S29	8	S14 AND (S10 OR S13) AND (S24 OR S25 OR S28)
S30	0	S29 NOT S18
S31	7	S14 AND S11 AND (S24 OR S25 OR S28)
S32	0	S31 NOT S18
S33	723	S1 AND (S10 OR S11 OR S13) AND (S15 OR S4 OR S8 OR S24 OR - S25 OR S28)
S34	364	S3 AND S33
S35	169	S1/TI,DE AND S34
S36	135	S35 NOT S18
S37	94	RD (unique items)
S38	27	S37/2001:2002
S39	32	S37/2003:2005
S40	35	S37 NOT S38:S39
S41	35	Sort S40/ALL/PY,A

23/7/1 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0009553926 BIOSIS NO.: 199598021759

Reverse remodeling : Chronic effects of cardiomyoplasty in failing human heart and role of external **constraint**

ASRC Searcher: Jeanne Horrigan
Serial 10/705989
March 18, 2005

4

AUTHOR: Kass David A; Pak Peter H; Baughman Kenneth L; Cho Peter; Acker Michael
AUTHOR ADDRESS: Johns Hopkins Med. Inst., Baltimore, MD, USA**USA
JOURNAL: Circulation 90 (4 PART 2): p1112 1994 1994
CONFERENCE/MEETING: 67th Scientific Sessions of the American Heart Association Dallas, Texas, USA November 14-17, 1994; 19941114
ISSN: 0009-7322
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English

23/7/2 (Item 2 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
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10948295 PMID: 7729016

Reverse remodeling from cardiomyoplasty in human **heart** failure. External **constraint** versus active **assist**.

Kass D A; Baughman K L; Pak P H; Cho P W; Levin H R; Gardner T J; Halperin H R; Tsitlik J E; Acker M A

Division of Cardiology, Johns Hopkins Medical Institutions, Baltimore, Md 21287, USA.

Circulation (UNITED STATES) May 1 1995, 91 (9) p2314-8, ISSN 0009-7322 Journal Code: 0147763

Contract/Grant No.: HL-47511; HL; NHLBI; RR00035; RR; NCRR

Publishing Model Print

Document type: Case Reports; Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

BACKGROUND: Cardiomyoplasty (CM) is a novel surgical therapy for **dilated** cardiomyopathy. In this procedure, the latissimus dorsi muscle is **wrapped** around the **heart** and chronically paced synchronously with **ventricular systole**. While studies have found symptomatic improvement from this therapy, the mechanisms by which CM confers benefit remain uncertain. This study sought to better define these mechanisms by means of serial pressure-volume relation analysis. METHODS AND RESULTS: Serial pressure-volume studies were performed by the conductance catheter method in three patients (total to date) with **dilated** cardiomyopathy (New York Heart Association class III) who underwent CM. Data were measured at baseline (before surgery) and at 6 and 12 months after CM. Chronic left **ventricular** (LV) **systolic** and **diastolic** **changes** induced by CM were evaluated with the stimulator in its stable pacing mode (every other beat) and after temporarily suspending pacing. CM-stimulated beats were compared with pacing-off beats to evaluate active **systolic assist** effects of CM. In each patient, CM resulted in a chronic lowering of **cardiac end-diastolic** volume and an increased ejection fraction. Most notably, the **end-systolic** pressure-volume relation shifted leftward, consistent with **reversal** of chronic chamber **remodeling**. In contrast, the **diastolic** pressure-volume relation was minimally altered, and the loops shifted down along the same baseline relation. These marked chronic **changes** in LV function measurable with CM stimulation off contrasted to only minor acute effects observed when the muscle **wrap** was activated. This suggests that the benefit of CM derived less from active **systolic assist** than from **remodeling**, perhaps because of an external elastic **constraint**.

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CONCLUSIONS: These data, while limited to a small number of patients, suggest that CM can **reverse remodeling** of the **dilated failing heart**. While **systolic** squeezing **assist** effects of CM may play a role in some patients, our study found that this was not required to achieve substantial benefits from the procedure. We speculate that CM may act more passively, like an elastic **girdle** around the **heart**, to help **reverse chamber remodeling**.

Record Date Created: 19950601

Record Date Completed: 19950601

23/7/3 (Item 3 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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11671823 PMID: 9064980

[Dynamic cardiomyoplasty: current status and concepts of the mechanism of action]

Dynamische Kardiomyoplastik: Aktueller Stand und Vorstellungen zum Wirkungsmechanismus.

Lange R; Hagl S

Abt. Herzchirurgie Chirurgische Universitätsklinik, Heidelberg.

Zeitschrift für Kardiologie (GERMANY) 1996, 85 Suppl 6 p309-15,

ISSN 0300-5860 Journal Code: 0360430

Publishing Model Print

Document type: Journal Article; Review; Review, Tutorial ; English
Abstract

Languages: GERMAN

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Surgical **treatment** of end-stage **heart** failure offers **heart** transplantation as a well established and effective **treatment** option. In addition, the permanent implantation of left-**heart assist**-devices is now gaining increasing importance. Yet, both methods also have inherent drawbacks and may not be available to all patients, so that new methods are constantly evaluated. Cardiomyoplasty was introduced into clinical practice 10 years ago, but still lacks general acceptance as a routine method. Worldwide results show a considerable symptomatic improvement with only small effects on **systolic cardiac** function. Survival rate was significantly improved by careful patient selection. As a mechanism of action the skeletal muscle **wrap** exerts some active improvement of **systolic** wall motion of the **heart/skeletal muscle-complex**. However, probably more important is an acute and chronically persisting shift of the pressure-volume relation to the left. This process results in a "**reverse remodeling**" of the insufficient **heart** with an improvement of the "**contractility reserve**". Cardiomyoplasty is indicated in patients with contraindications to **heart** transplantation and as a bridge-to-transplantation in patients with **ventricular** arrhythmia and severely impaired left **ventricular** function, concomitant with ICD implantation. (25 Refs.)

Record Date Created: 19970319

Record Date Completed: 19970319

23/7/5 (Item 5 from file: 73)

DIALOG(R) File 73:EMBASE

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07341272 EMBASE No: 1998245552

Remodeling of cardiac membranes during the development of congestive heart failure

Dhalla N.S.; Shao Q.; Panagia V.

Dr. N.S. Dhalla, Institute of Cardiovascular Sciences, St. Boniface Gen. Hosp. Res. Center, 351 Tache Avenue, Winnipeg, Man. R2H 2A6 Canada

Heart Failure Reviews (HEART FAIL. REV.) (Netherlands) 1998, 2/4 (261-272)

CODEN: HFREF ISSN: 1382-4147

DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 125

Various proteins such as Casup 2sup + channels, Casup 2sup +-pump ATPase, Nasup +- Casup 2sup + exchanger, and Nasup +-Ksup + ATPase in the sarcolemmal (SL) membrane are considered to be intimately involved in Casup 2sup +-influx and Casup 2sup +-efflux processes in the cardiomyocyte. On the other hand, Casup 2sup +-pump ATPase, Casup 2sup +-release channels, Casup 2sup +-regulatory protein (phospholamban), and Casup 2sup +- **binding** protein (calsequestrin) in the sarcoplasmic reticulum (SR) are known to participate in raising and lowering the intracellular concentration of Casup 2sup + for the occurrence of **cardiac contraction** and relaxation processes. Therefore, a defect in any of the SL and SR proteins can be seen to result in Casup 2sup +-handling abnormalities in cardiomyocytes and subsequently in **cardiac** dysfunction during the development of **heart failure**. In this review, evidence is presented to show that **changes** in the expression of genes specific for **cardiac** membrane proteins may lead to **remodeling** of both SR and SL membranes during the development of **heart failure**. Although a great deal of work on **changes** in gene expression for the SR membrane proteins has been carried out in the failing **heart**, relatively little information regarding **changes** in gene expression for SL proteins has appeared in the literature. **Prevention of remodeling of cardiac** membranes by modification of **changes** in the gene expression is suggested to serve as an important target for the **treatment of heart failure**.

23/7/6 (Item 6 from file: 155)

DIALOG(R) File 155:MEDLINE(R)

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12263795 PMID: 9573504

Surgical approaches to arresting or reversing chronic remodeling of the failing heart.

Kass D A

Department of Medicine, Johns Hopkins Medical Institutions, Baltimore, MD 21287, USA.

Journal of cardiac failure (UNITED STATES) Mar 1998, 4 (1) p57-66, ISSN 1071-9164 Journal Code: 9442138

Publishing Model Print

Document type: Journal Article; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Chronic **ventricular remodeling** is a central feature of **heart** failure that strongly correlates with a poor prognosis. Several recent surgical **treatments** for **heart** failure may derive benefit by their ability to arrest or substantially **reverse** this **remodeling** process. Dynamic cardiomyoplasty involves **wrapping** the **heart** with the latissimus dorsi muscle and stimulating the muscle to **assist** contraction. The **wrap** itself may provide a **constraint** helping to **limit** progressive **cardiac** **dilation** and/or **assist** in **reversing** this process. Left **ventricular assist** devices almost completely unload the **heart** and **augment** systemic circulation, thereby reducing neurohumoral activation. These combined effects seem to alter the chamber and cellular phenotype, and **reversal** of some molecular **changes** are associated with failure. Lastly, the partial ventriculectomy procedure directly **reverses** **remodeling** by acute removal of a portion of the lateral wall. Only preliminary nonrandomized trial data are currently available for each of these therapies with larger trials under way. However, early results are intriguing and are yielding insights into these mechanisms. (63 Refs.)

Record Date Created: 19980702

Record Date Completed: 19980702

41/7/10 (Item 10 from file: 73)
DIALOG(R) File 73:EMBASE
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06636461 EMBASE No: 1996301273
Mechanisms of dynamic cardiomyoplasty: Current concepts
Oh J.H.; Badhwar V.; Chiu R.C.-J.
Montreal General Hospital, 1650 Cedar Avenue, Montreal, Que. H3G 1A4
Canada
Journal of **Cardiac** Surgery (J. CARD. SURG.) (United States) 1996, 11/3
(194-199)
CODEN: JCASE ISSN: 0886-0440
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Dynamic cardiomyoplasty is an operation that is undergoing worldwide clinical evaluation. It had been developed to utilize the patient's own skeletal muscle to **assist** the failing **heart**. Although the clinical and quality of life benefits of cardiomyoplasty have been reported in most patients, the results of quantitative hemodynamic analyses have been less consistent. This has prompted the reevaluation of the mechanisms of dynamic cardiomyoplasty other than simple **cardiac** compression by the **wrapped** muscle. There is good evidence to suggest that the following, either together or in part, comprise some of the mechanisms of dynamic cardiomyoplasty: (1) direct **systolic assist**; (2) myocardial (wall stress) sparing effect; (3) **remodeling** / **girdling** effect; and (4) angiogenesis. Current concepts and potential additional mechanisms are discussed and integrated, based on a review of the literature and our own recent studies.

41/7/11 (Item 11 from file: 34)
DIALOG(R) File 34:SciSearch(R) Cited Ref Sci
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05299389 Genuine Article#: VN754 Number of References: 156

Title: MEDICAL THERAPY CAN IMPROVE THE BIOLOGICAL PROPERTIES OF THE
CHRONICALLY FAILING **HEART** - A NEW ERA IN THE **TREATMENT** OF **HEART**
-FAILURE

Author(s): EICHHORN EJ; BRISTOW MR

Corporate Source: UNIV TEXAS,VET ADM MED CTR,**CARDIAC** CATHETERIZATLAB
IIIA2,4500 S LANCASTER/DALLAS//TX/75216; UNIV TEXAS,SW MED CTR,DEPT
INTERNAL MED,DIV CARDIOL/DALLAS//TX/00000; UNIV COLORADO,HLTH SCI
CTR,DIV CARDIOL/DENVER//CO/80262; UNIV TEXAS,VET ADM MED CTR,**CARDIAC**
CATHETERIZATLAB IIIA2/DALLAS//TX/75216

Journal: CIRCULATION, 1996, V94, N9 (NOV 1), P2285-2296

ISSN: 0009-7322

Language: ENGLISH Document Type: REVIEW

Abstract: Myocardial failure has been considered to be an irreversible and progressive process characterized by **Ventricular** enlargement, chamber geometric alterations, and diminished pump performance. However, more recent evidence has suggested that certain types of medical therapy may lead to retardation and even **reversal** of the cardiomyopathic process. In the failing **heart**, long-term neurohormonal/autocrine-paracrine activation results in abnormalities in myocyte growth, energy production and utilization, calcium flux, and receptor regulation that produce a progressively dysfunctional, mechanically inefficient **heart**. Interventions such as ACE inhibition and beta-blockade result in a reduction in the harmful long-term consequences of neurohormonal/autocrine-paracrine effects and retard the progression of left **ventricular** dysfunction or **ventricular remodeling**. Furthermore, in subjects with idiopathic **dilated** or ischemic cardiomyopathy, antiadrenergic therapy with beta-blocking agents appears to be able to partially **reverse systolic** dysfunction and **ventricular remodeling**. Although the precise mechanisms underlying this latter effect have not yet been elucidated, the general mechanism appears to be via improvement in the biological function of the **cardiac** myocyte. Such an improvement in the intrinsic defect(s) responsible for myocardial failure will likely translate into important clinical benefits.

41/7/15 (Item 15 from file: 34)

DIALOG(R) File 34:SciSearch(R) Cited Ref Sci

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05719393 Genuine Article#: WT449 Number of References: 17

Title: Dynamic cardiomyoplasty: Insights into the mechanisms of its success

Author(s): Patel HJ; Lankford EB; Polidori DJ; Pilla JJ; Acker MA

(REPRINT)

Corporate Source: HOSP UNIV PENN,DIV CARDIOTHORAC SURG, 34TH & SPRUCE ST,
SILVERSTEIN 6/PHILADELPHIA//PA/19104 (REPRINT); UNIV PENN,SCH MED, DEPT
SURG/PHILADELPHIA//PA/19104; UNIV PENN,SCH MED, DEPT
MED/PHILADELPHIA//PA/19104

Journal: BASIC AND APPLIED MYOLOGY, 1997, V7, N1, P5-7

ISSN: 1120-9992 Publication date: 19970000

Publisher: UNIPRESS PADOVA, 231 VIA C BATTISTI, 35123 PADOVA, ITALY

Language: English Document Type: ARTICLE

Abstract: Dynamic cardiomyoplasty is a recently developed operation for the **treatment** of end-stage **heart** failure. Recent studies have focused on the potential mechanism by which it may work. We have shown in a canine

model of **heart** failure, using transformed muscle, that CMP has at least two mechanisms. First, it stabilizes **ventricular** function and volumes chronically by a **girdling** mechanism. Secondly, dynamic **assistance** acts acutely to **augment systolic contraction**. These two mechanisms act to stabilize **cardiac** function and may potentially allow for **reversal** of the chronic **remodeling** process seen with progressive **heart** failure.

41/7/17 (Item 17 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
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12097096 PMID: 9396469

Stabilization of chronic **remodeling** by asynchronous cardiomyoplasty in **dialted** cardiomyopathy: effects of a conditioned muscle **wrap**.

Patel H J; Polidori D J; Pilla J J; Plappert T; Kass D; St John Sutton M; Lankford E B; Acker M A

Department of Surgery, University of Pennsylvania School of Medicine, Philadelphia 19104, USA.

Circulation (UNITED STATES) Nov 18 1997, 96 (10) p3665-71, ISSN 0009-7322 Journal Code: 0147763

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

BACKGROUND: Dynamic cardiomyoplasty is a promising new therapy for **dialted** cardiomyopathy. The **girdling** effects of a conditioned muscle **wrap** alone have recently been postulated to partly explain its mechanism. We investigated this effect in a canine model of chronic **dialted** cardiomyopathy. METHODS AND RESULTS: Twenty dogs underwent rapid **ventricular** pacing (RVP) for 4 weeks to create a model of **dialted** cardiomyopathy. Seven dogs were then randomly selected to undergo subsequent cardiomyoplasty, and all dogs had 6 weeks of additional RVP. The cardiomyoplasty group also received 6 weeks of concurrent skeletal muscle stimulation consisting of single twitches delivered asynchronously at 2 Hz to transform the **wrap** without active **assistance**. All dogs were studied by pressure-volume analysis and echocardiography at baseline and after 4 and 10 weeks of pacing. **Systolic** indices, including ejection fraction (EF), end- **systolic** elastance (Ees), and preload-recrutable stroke work (PRSW) were all increased at 10 weeks in the **wrap** versus controls (EF, 34.0 versus 27.1, P=.008; Ees, 1.65 versus 1.26, P=.09; PRSW, 35.9 versus 25.5, P=.001). **Ventricular** volumes, **diastolic** relaxation, and left **ventricular** end- **diastolic** pressures stabilized in the cardiomyoplasty group but continued to deteriorate in controls. Both the end- **systolic** and end- **diastolic** pressure-volume relationships shifted farther rightward in controls but remained stable in the cardiomyoplasty group. CONCLUSIONS: In addition to potential benefits from active **systolic assistance**, benefits from dynamic cardiomyoplasty appear to be partially accounted for by the presence of a conditioned muscle **wrap** alone. This conditioned **wrap** stabilizes the **remodeling** process of **heart** failure, arresting progressive deterioration of **systolic** and **diastolic** function.

Record Date Created: 19980109

Record Date Completed: 19980109

41/7/23 (Item 23 from file: 155)
DIALOG(R) File 155:MEDLINE(R)
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13504431 PMID: 10475482

Dynamic cardiomyoplasty: at the crossroads.

Acker M A

Division of Cardiothoracic Surgery, University of Pennsylvania School of Medicine, Philadelphia, USA. macker@mail.med.upenn.edu

Annals of thoracic surgery (UNITED STATES) Aug 1999, 68 (2) p750-5, ISSN 0003-4975 Journal Code: 15030100R

Publishing Model Print

Document type: Clinical Trial; Clinical Trial, Phase III; Journal Article; Randomized Controlled Trial; Review; Review, Tutorial

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

BACKGROUND: Dynamic cardiomyoplasty remains a promising, but still unproven surgical **treatment** for patients with end-stage **heart** failure. Lack of a clear survival advantage and ongoing misunderstanding of its mechanism of action have hindered its acceptance as a **treatment** alternative for patients with end-stage **heart** failure. This review seeks to update current clinical results and practice of dynamic cardiomyoplasty and to present its likely mechanism of action. METHODS: The method involved a literature review. RESULTS: More than 600 patients have undergone dynamic cardioplasty since 1985. Improvement in average New York **Heart** Association class was noted in 80% to 85% of hospital survivors. Operative mortality has decreased from 31% in Phase I to less than 3% in the ongoing Phase III trial. Clinical work as well as recent animal work supports the hypothesis that through a combination of long-term elastic **constraint** and active dynamic **assist**, dynamic cardiomyoplasty decreases myocardial wall stress associated with the **remodeling** process of progressive **heart** failure. CONCLUSIONS: Though dynamic cardiomyoplasty can be shown to **limit** the **remodeling** process of **heart** failure in animal studies and some patients, its ultimate role in the **treatment** of **heart** failure will depend on the outcome of randomized, controlled studies. (38 Refs.)

Record Date Created: 19990915

Record Date Completed: 19990915

Serial 10/705989

March 18, 2005

File 350:Derwent WPIX 1963-2005/UD,UM &UP=200518

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File 347:JAPIO Nov 1976-2004/Nov(Updated 050309)

(c) 2005 JPO & JAPIO

Set	Items	Description
S1	2695	REMODELING
S2	4353257	REVERS??? OR TREAT? OR PREVENT?
S3	45305	HEART OR CARDIAC()APEX OR VENTRICLE OR VENTRICULAR OR PERI-CARDI? OR EPICARDI?
S4	1569	DIASTOLE OR DIASTOLIC
S5	2203483	RESIST? OR LIMIT???
S6	763502	STRETCH??? OR DISTENTION OR DISTENT??? OR STRAIN??? OR SWE-LL??? OR DIALT??? OR EXPAND??? OR EXPANSION
S7	10077	SHAPE(1N)CHANG???
S8	109891	SYSTOLE OR SYSTOLIC OR CONTRACT???
S9	1043703	AUGMENT? OR AID??? OR ASSIST? OR FORCE
S10	85261	HARNES OR HARNESSES OR JACKET? ? OR SOCK? ? OR GIRDLE? ? - OR GIRDLING ORWRAP? ? OR SPLINT? ?
S11	435728	BIND??? OR BOUND OR CONSTRAINT? ?
S12	41578	GIRDLING OR WRAP? ?
S13	1316	DISTEND???
S14	6	S2(1W)S1 AND S10:S12
S15	1417	S10:S12(S)S3
S16	24	S4 AND S8 AND S15
S17	23	S16 NOT S14
S18	9490	S5(1N)(S6:S7 OR S13)
S19	1301	S9(1N)S8
S20	458759	ELASTIC?
S21	11	S15 AND S18:S19
S22	6	S21 NOT (S14 OR S16)
S23	18	S20(S)S15
S24	14	S23 NOT (S14 OR S16 OR S21)

14/34/6 (Item 6 from file: 350)

DIALOG(R)File 350:Derwent WPIX

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012814036 **Image available**

WPI Acc No: 1999-620267/199953

Method of implanting a long term **cardiac** support device in a **pericardial** sac for a failing **heart**

Patent Assignee: SNYDERS R V (SNYD-I); CARDIO TECHNOLOGIES INC (CARD-N)

Inventor: SNYDERS R V

Number of Countries: 086 Number of Patents: 006

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 9952470	A1	19991021	WO 99US7726	A	19990409	199953 B
AU 9932223	A	19991101	AU 9932223	A	19990409	200013
US 6095968	A	20000801	US 9881286	P	19980410	200039
			US 99288488	A	19990408	
JP 2002511305	W	20020416	WO 99US7726	A	19990409	200242
			JP 2000543083	A	19990409	
AU 758285	B	20030320	AU 9932223	A	19990409	200329
MX 2000009927	A1	20020401	WO 99US7726	A	19990409	200363
			MX 20009927	A	20001010	

Priority Applications (No Type Date): US 9881286 P 19980410; US 99288488 A 19990408

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 9952470 A1 E 19 A61F-002/04

Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW

AU 9932223 A Based on patent WO 9952470

US 6095968 A A61M-001/12 Provisional application US 9881286

JP 2002511305 W 17 A61F-002/04 Based on patent WO 9952470

AU 758285 B A61F-002/04 Previous Publ. patent AU 9932223

Based on patent WO 9952470

MX 2000009927 A1 A61F-002/04 Based on patent WO 9952470

Abstract (Basic): WO 9952470 A1

NOVELTY - Method of implanting a long term **cardiac** support in a **pericardial** sac includes enclosing a **heart** within the **pericardial** sac with the support device having an outer inelastic ply and an inner lining ply which abuts the **ventricular** masses of the **heart**; instilling a viscous fluid between the inelastic ply and the elastic lining ply; and monitoring the pressure of the viscous fluid in the device.

USE - The invention is useful for individuals suffering from certain late-stage **heart** failure disease entities, e.g. **dilated** cardiomyopathies.

ADVANTAGE - Diminutive fabrication features of the device showed that it is quite easily adjustable to any **cardiac** size and is virtually self-sizing relative to circumferential dimension requirements even for the very largest **hearts** for insertion around the **heart** and inside the **pericardial** sac. Subsequent filling of the sac space with a viscous silicone or other equivalent non-compressible fluid through the fill line of the device results in a viscous cardioplasty reinforcement of the thinned **ventricular** walls resulting to a reduction in LV and RV diameters to effect a desirable reduction of wall stress, which consequently provides for an effective **reverse remodeling** of the **heart** via both **diastolic** and **systolic** volumetric restriction but not constriction of the **ventricular** anatomy and with a subsequent improved physiological benefit to **cardiac** function.

DESCRIPTION OF DRAWING(S) - The figure is a frontal perspective view showing the entire **heart** and great vessels with the right and left **ventricles** enveloped by the **Ventricular Assist Device jacket** closely fitted within the **pericardial** sac.

Device (10)

Inelastic elastomeric biocompatible material (12)

Conduit fill line (7)

Pericardial sac (19)

pp; 19 DwgNo 5/5

Technology Focus:

TECHNOLOGY FOCUS - MECHANICAL ENGINEERING - Preferred Device: The inelastic ply is adjustable to facilitate circumferential fitting of the device to the **heart**. The device has a diminutive structural dimension so that the **pericardial** sac can be saved with an ideally congruent fit of the device within the **pericardial** sac which allows a

free choice of closure of the **pericardial** sac. The device further includes a conduit fill line, an implantible reservoir having a junction with the conduit fill line, an adapter syringe attached to a fluid reservoir and to the conduit fill line, and an operable valve in the junction of the flexible reservoir and the fill line for charging fluid from the reservoir to the device.

Preferred Method: No or minimal pressurization in the device is registered with the result of a viscous cardioplasty reinforcement of the **ventricular** wall with a resultant reduction in left and right **ventricular** diameters and volumes to effect reduction of wall stress, thus effectively **remodeling** the **diastolic** and **systolic** volumetric character of the **heart** anatomy. The viscous fluid is instilled in simple gravity fill without requiring any superseding pressure. Minimal pressurization of 2-10 mmHg is developed within the device above the gravity fill at atmospheric pressure. A fluid reservoir for the fluid fill is provided and implanted in the upper abdominal subcutaneous space for refilling of the device. The fluid fill line includes a flexible portion to allow free positioning of the fill line. The device may be filled by a syringing flow from an external viscous fluid container and the fill line is plugged for revisiting in the subcutaneous site.

POLYMERS - Preferred Fluid: The viscous fluid is a high viscosity silicone biocompatible liquid preferably polydimethylsilicone, fluoropropylsilicone, or equivalent high viscosity fluid of similar density. The viscous fluid has a specific gravity of 0.97 or 0.98.

Derwent Class: A26; A96; D22; P32; P34

International Patent Class (Main): A61F-002/04; A61M-001/12

17/26, TI/15 (Item 15 from file: 350)
DIALOG(R) File 350: Derwent WPIX
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013908399

WPI Acc No: 2001-392612/200142

Left- **ventricular** sack for pumping blood from left- **ventricular** section in artificial-organ development, comprises an elastic rubber cord which spirally **wraps** periphery of sack main body in the form of a shell

17/34/20 (Item 20 from file: 350)
DIALOG(R) File 350: Derwent WPIX
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013011018 **Image available**

WPI Acc No: 2000-182870/200016

Transventricular splint for reducing wall stress of failing **heart** has elongate tension member of specified length with atraumatic anchors at each end

Patent Assignee: MYOCOR INC (MYOC-N)

Inventor: KEITH P T; MORTIER T J; PAULSON T M; SCHWEICH C J; VIDLUND R M

Number of Countries: 087 Number of Patents: 006

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200006026	A2	20000210	WO 99US16874	A	19990727	200016 B
US 6045497	A	20000404	US 97778277	A	19970102	200024
			US 97933456	A	19970918	

			US 98124286	A	19980729	
AU 9952308	A	20000221	AU 9952308	A	19990727	200029
US 6261222	B1	20010717	US 97778277	A	19970102	200142
			US 97933456	A	19970918	
			US 98124286	A	19980729	
			US 2000497118	A	20000203	
EP 1143858	A2	20011017	EP 99937483	A	19990727	200169
			WO 99US16874	A	19990727	
US 6629921	B1	20031007	US 97778277	A	19970102	200374
			US 97933456	A	19970918	
			US 98124286	A	19980729	
			US 2000497118	A	20000203	
			US 2000697711	A	20001027	

Priority Applications (No Type Date): US 98124286 A 19980729; US 97778277 A 19970102; US 97933456 A 19970918; US 2000497118 A 20000203; US 2000697711 A 20001027

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200006026	A2	E	46	A61B-017/00	
					Designated States (National): AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW
					Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW
US 6045497	A			A61B-017/12	CIP of application US 97778277 CIP of application US 97933456
AU 9952308	A				Based on patent WO 200006026
US 6261222	B1			A61M-031/00	CIP of application US 97778277 CIP of application US 97933456 Cont of application US 98124286 CIP of patent US 5961440 Cont of patent US 6045497 CIP of patent US 6050936
EP 1143858	A2	E		A61B-017/00	Based on patent WO 200006026
					Designated States (Regional): AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
US 6629921	B1			A61M-031/00	CIP of application US 97778277 CIP of application US 97933456 Cont of application US 98124286 Cont of application US 2000497118 CIP of patent US 5961440 Cont of patent US 6045497 CIP of patent US 6050936

Abstract (Basic): WO 200006026 A2

NOVELTY - The transventricular splint has an elongate tension member (16) with atraumatic anchors (20) at each end. The member is 1-4 inches long between the anchors. The tension member may 0.01 - 0.02 inches diameter and 0.6 - 2.0 inches long. It may be a multi-filament with a radiopaque marker and an antithrombogenic coating. Alternatively it may be an echo cardiograph.

USE - Reducing the wall stress of a failing heart during diastole and systole.

ADVANTAGE - The device is a passive non-pharmalogical apparatus

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March 18, 2005

that reduces the energy consumption of the failing **heart**.

DESCRIPTION OF DRAWING(S) - The figure shows a transverse cross-section of the left and right **ventricles** of a human **heart** showing the placement of a splint .

Elongate tension member (16)

Atraumatic anchors (20)

pp; 46 DwgNo 1/40

Derwent Class: B07; P31; P34

International Patent Class (Main): A61B-017/00; A61B-017/12; A61M-031/00

17/34/23 (Item 23 from file: 350)

DIALOG(R) File 350:Derwent WPIX

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009072544 **Image available**

WPI Acc No: 1992-199963/199224

Copulsation and counter-pulsation **cardiac assist** appts. - uses train of pulses to activate each of the muscles in alternate fashion to **contract** respective muscles

Patent Assignee: UNIV MCGILL (UYMC-N)

Inventor: CHIU R C; CHIU R C J

Number of Countries: 016 Number of Patents: 002

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 9208500	A1	19920529	WO 90CA390	A	19901109	199224 B
US 5429584	A	19950704	WO 90CA390	A	19901109	199532
			US 9350392	A	19930818	

Priority Applications (No Type Date): WO 90CA390 A 19901109

Cited Patents: EP 216042; FR 2220279; FR 2321266; GB 1528072; US 4192293; US 4453537

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 9208500 A1 E 15 A61M-001/12

Designated States (National): CA JP US

Designated States (Regional): AT BE CH DE DK ES FR GB GR IT LU NL SE

US 5429584 A 10 A61M-001/10 Based on patent WO 9208500

Abstract (Basic): WO 9208500 A

The copulsation and counterpulsation **cardiac assist** apparatus comprises copulsation and counterpulsation devices. The copulsation device includes a peri-**cardiac assist** device, including a fluid expansible envelope for compressing the **heart** during **systole** . The counterpulsation device performs a number of functions including a fluid expansible balloon for compressing a portion of the aorta during **diastole** . A muscle powered fluid pressure device supplies alternating fluid pressure to the copulsation and the counterpulsation devices. The **heart** rate is sensed and a stimulating pulse is produced to stimulate the selected muscles to **contract** . A reciprocating pump enables fluid pressure flows from one chamber to the other.

USE/ADVANTAGE - Combined peri-**cardiac** implant. Provides co-ordinated and combined totally implantable muscle powered peri-**cardiac** cup copulsation device.

Dwg. 1,2/6

Abstract (Equivalent): US 5429584 A

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March 18, 2005

The co-pulsation and counter-pulsation **cardiac assist** appts. has a co-pulsation device including a peri-**cardiac assist** device with a fluid expansible envelope for compressing the **heart** during **systole**, and a counter-pulsation device comprising a peri-aortic **jacket** including a fluid expansible balloon for compressing a portion of the aorta during **diastole**. A muscle powered fluid pressure device supplies alternating fluid pressure to the co-pulsation and counter-pulsation devices.

A detector senses the **heart** rate and a pulse generator produces a stimulating pulse to selected muscles to **contract** them w.r.t. signals from the pressurising device. A negative pressure booster has adjacent separate flow chambers through which the alternating fluid pressures flow, and a reciprocating pump has at least a pump element in each chamber, such that when the fluid pressure flows through one chamber, it causes a pump to provide a negative pressure in the other chamber to enhance withdrawal of the fluid from a respective one of the co-pulsation and the counter-pulsation devices.

ADVANTAGE - Improved **heart** rate response control.

Dwg.2/6

Derwent Class: P33; P34; S05

International Patent Class (Main): A61M-001/10; A61M-001/12

International Patent Class (Additional): A61H-031/00

22/34/1 (Item 1 from file: 350)

DIALOG(R) File 350:Derwent WPIX

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016818608

WPI Acc No: 2005-142891/200515

Implantable synthetic tissue or tissue complex useful for **treating heart** failure, myocardial infarct or disorder of bone, cartilage and ligament, comprises implantable synthetic tissue and another synthetic tissue

Patent Assignee: NAKAMURA N (NAKA-I)

Inventor: ANDO W; MATSUDA H; MIYAGAWA S; NAKAMURA N; SAWA Y; TAKETANI S;

YOSHIKAWA H

Number of Countries: 108 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
WO 200512512	A1	20050210	WO 2004JP11401	A	20040802	200515 B

Priority Applications (No Type Date): JP 200458285 A 20040302; JP

2003285475 A 20030801

Patent Details:

Patent No Kind Lan Pg Main IPC Filing Notes

WO 200512512 A1 E 459 C12N-005/06

Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ
CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID
IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ
NA NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ
UA UG US UZ VC VN YU ZA ZM ZW

Designated States (Regional): AT BE BG BW CH CY CZ DE DK EA EE ES FI FR
GB GH GM GR HU IE IT KE LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL
SZ TR TZ UG ZM ZW

Abstract (Basic): WO 200512512 A1

NOVELTY - An implantable synthetic tissue (I) or a tissue complex

comprising an implantable synthetic tissue and another synthetic tissue.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) producing (M1) a synthetic tissue, involves providing cells, placing the cells in a container having cell culture medium comprising an extracellular matrix (ECM) synthesis promoting agent and having a sufficient base area which can accommodate a synthetic tissue having a desired size, culturing the cells in the container along with the cell culture medium containing the ECM synthesis promoting agent for a period of time sufficient for formation of the synthetic tissue having the desired size, and detaching the cells from the container, optionally regulating the thickness of synthetic tissue by physical or chemical stimulus to a desired thickness;

(2) a cell culture composition for producing a synthetic tissue from cells, comprising an element for maintaining the cells, and an extracellular matrix synthesis promoting agent;

(3) a complex (II) for reinforcing a portion of an organism, comprising cells and a component derived from the cells;

(4) reinforcing (M2) a portion of an organism, involves replacing the portion with a complex comprising cells and a component derived from the cells or providing the complex to cover the portion, or both, and holding the complex for a sufficient period of time for biologically adhering the complex to the portion;

(5) **treating** (M3) a portion of an organism, involves carrying out (M2); and

(6) a composition for use in producing synthetic tissue having a desired thickness, comprising a chemical substance chosen from actin depolymerizing agents and actin polymerizing agents.

ACTIVITY - Cardiant; Vasotropic; Cardiovascular; Osteopathic. The ability of synthetic tissue to **treat** myocardial infarction was determined in vivo. The synthetic tissue was produced in the presence of ascorbic acids and was implanted into a **dialted** cardiomyopathy rat. The left anterior descending (LAD) was ligated for 2 weeks to produce injured **hearts**. The synthetic tissue was implanted into some of the injured **hearts**. As controls, rats without injury to their **hearts** were obtained. The rats were anesthetized and operated. The **heart** function of the rats was monitored on Day 14 and 28 after surgery. Two and four weeks after implantation, the rats were sacrificed with an excessive amount of pentobarbital. The **heart** was dissected, fixed with 10% formalin, and embedded in paraffin. A series of sections having a thickness of 5 mm were prepared. All of the rats with implants were completely cured, and survived for substantially the same period of time as normal rats. Therefore, it was demonstrated that the synthetic tissue can completely cure diseases in the presence of a specific ECM synthesis promoting agent.

MECHANISM OF ACTION - Cell-Therapy.

USE - (I) is useful for implantation of cells. (M2) is useful for reinforcing a portion of an organism, where the portion is a **heart** having a disease or disorder chosen from **heart** failure, ischemic **heart** disease, myocardial infarct, cardiomyopathy, myocarditis, hypertrophic cardiomyopathy, **dialted** phase hypertrophic cardiomyopathy and **dialted** cardiomyopathy. The portion includes avascular lesion, vascular lesion, bone, cartilage, intervertebral disk, meniscus, ligament or tendon, damaged or degenerated bone or cartilage, intractable fracture, osteonecrosis, cartilage injury, meniscus injury, ligament injury,

tendon injury, cartilage degeneration, meniscus degeneration, intervertebral disk denaturation, ligament degeneration or tendon degeneration. (M3) is useful for **treating**, **preventing**, or reinforcing a disease, disorder, or condition of **heart**, bone, cartilage, ligament, tendon, meniscus or intervertebral disk (all claimed).

ADVANTAGE - (I) is large sized, having a volume of 20 mm³, is flexible, **expandable** and **contractile**, and can withstand **heart** pulsation (claimed). (I) is highly safe and does not cause any side effects when used in **treatment**.

pp; 459 DwgNo 0/46

Technology Focus:

TECHNOLOGY FOCUS - BIOTECHNOLOGY - Preferred Synthetic Tissue: (I) is biologically organized in the third dimensional direction. (I) has biological integration capability with surroundings, such as capability to adhere to surrounding cells and/or extracellular matrices. (I) comprises cells and is substantially made of cells and a material derived from the cells or ECM derived from the cells. The ECM contains collagen I, collagen III, vitronectin and fibronectin, preferably vitronectin and fibronectin. The ECM contains collagen I and collagen III, where the collagen constitutes 5-25% of the tissues, and the ratio of the collagen I to collagen III is between 1:10 and 10:1. The ECM and the cells are integrated together into a three-dimensional structure. The ECM is diffusely distributed in the tissue and the distribution densities of the ECM in two arbitrary sections of 1 cm² in the tissue have a ratio within a range of 1:3-3:1. (I) is heterologous, allogenic, isologous, or autogenous. (I) is free of scaffolds. (I) is biologically organized in all three-dimensional directions. The biological integration is chosen from internal **binding** of extracellular matrix, electrical integration, and intercellular signal transduction. (I) has a tissue strength, which allows the synthetic tissue to be clinically applicable. The strength is a break strength of 0.02-2 N. The tissue strength is sufficient to provide self-supporting ability, where the self-supporting ability is the capability of synthetic tissue to remain unbroken when the synthetic tissue is picked up using **forceps** having a tip area of 0.05-3 mm², or with a hand. The site to which the synthetic tissue is intended to be applied includes **heart**, intervertebral disk, meniscus, cartilage, bone, ligament or tendon, where the synthetic tissue remains attached without an additional fixation procedure, after the synthetic tissue is implanted into an injured portion of the intra-articular tissue. In (I), the implantable synthetic tissue is biologically integrated with the other synthetic tissue by an extracellular matrix.

Preferred Method: In (M1), the stimulus for inducing tissue **contraction** is applied in the detaching step. The stimulus includes a physical or chemical stimulus. The physical stimulus includes shaking of the container, pipetting or deformation of the container. The detaching step includes adding an actin regulatory agent, which comprises a chemical substance chosen from actin depolymerizing agents and actin polymerizing agents. The actin depolymerizing agent is chosen from Slingshot, cofilin, cyclase associated protein (CAP), actin interacting protein 1 (AIP1), actin depolymerizing factor (ADF), destrin, depactin, actophorin, cytochalasin and nerve growth factor (NGF). The actin polymerizing agent is chosen from RhoA, mDi, profilin, Rac1, IRSp53, WAVE2, ROCK, LIM kinase, cofilin, cdc42, N-WASP, Arp2/3, Drf3, Mena, lysophosphatidic acid (LPA), insulin, platelet derived growth factor-a ((PDGF)-a), PDGF-b, chemokine and transforming growth

factor (TGF)-(beta). The chemical stimulus is obtained by using a chemical substance chosen from actin depolymerizing agents and actin polymerizing agents. The container is free of scaffolds. The cells are first cultured in monolayer culture. The ECM synthesis promoting agent includes TGFbeta1, TGFbeta3, ascorbic acid, ascorbic acid 2-phosphate, or its derivatives or salts. The ascorbic acid, ascorbic acid 2-phosphate, or its derivative or salt is present at a concentration of 0.1 mM. The TGFbeta1 or TGFbeta3 is present at a concentration of 1 ng/ml. The cells are placed at a concentration of 5×10^4 to the power 6 cells/cm squared. (M1) further involves causing the synthetic tissue to detach from the container and self-**contract**, and causing the synthetic tissue to differentiate, where the detaching and self-**contraction** are achieved by providing a physical stimulus or chemical stimulus to the container. The culturing step is carried-out for a sufficient period of 3 days and a period of time required for the synthetic tissue to be spontaneously detached from the container at a maximum, which is at least 40 days. The differentiation includes osteogenesis, chondrogenesis, adipogenesis, tendon differentiation and ligament differentiation. The osteogenesis is performed in medium containing dexamethasone, beta-glycerophosphate and ascorbic acid 2-phosphate. The medium contains any one of bone morphogenetic protein-2 (BMP-2), BMP-4, BMP-7, TGF-beta1 and TGF-beta3. The chondrogenesis is performed in medium containing pyruvic acid, dexamethasone, ascorbic acid 2-phosphate, insulin, transferring and selenious acid. The differentiation step is performed before or after the detaching step, preferably after the detaching step. The cell includes cells of 3 or more passages, preferably 3-8 passages. The cells include myoblasts, fat-derived cells, synovium-derived cells and mesenchymal stem cells, which are derived from an adipose tissue, synovial membrane, a tendon, bone or bone marrow. (M1) further involves producing several synthetic tissues and attaching the synthetic tissues together to be integrated. The desired thickness is regulated by adjusting a ratio of the actin depolymerizing agent to the actin polymerizing agent. In (M2), the ECM is provided on a surface of the complex, or diffusely distributed on a surface of the complex. (M2) further involves forming the complex by culturing the cells in the presence of an ECM synthesis promoting agent and implanting another synthetic tissue. In (M2), the complex is held for a sufficient period of time, which is at least 10 days. The other synthetic tissue is an artificial bone or a microfibrillar collagen medical device. The complex is substantially made of cells and an ECM derived from the cells. The artificial bone includes hydroxyapatite.

Preferred Complex: In (II), the portion includes avascular tissue, intravertebral disk, meniscus, ligament or tendon. The reinforcement is achieved by replacing the portion with the complex or providing the complex to cover the portion, or both. (II) **resists** the **expansion** and **contraction** of the portion.

Extension Abstract:

EXAMPLE - No relevant example is given.

Derwent Class: B04; D16; D22

International Patent Class (Main): C12N-005/06

22/34/2 (Item 2 from file: 350)

DIALOG(R) File 350:Derwent WPIX

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Serial 10/705989

March 18, 2005

013843223 **Image available**

WPI Acc No: 2001-327436/200134

Passive **girdle** includes **wrap** member with **constraining** material that **resists heart expansion** beyond one of preset inner perimeters or **wrap** member without **resisting systolic** ejection

Patent Assignee: ABIOMED INC (ABIO-N)

Inventor: KUNG R T V; LEDERMAN D M

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 6224540	B1	20010501	US 95490080	A	19950613	200134 B
			US 95581051	A	19951229	
			US 9823592	A	19980213	

Priority Applications (No Type Date): US 95581051 A 19951229; US 95490080 A 19950613; US 9823592 A 19980213

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 6224540	B1	10	A61F-002/04		CIP of application US 95490080 Div ex application US 95581051 CIP of patent US 5713954 Div ex patent US 5800528

Abstract (Basic): US 6224540 B1

NOVELTY - The **girdle** (17) includes a **wrap** member that conformingly surrounds at least a portion of the circumference of the **heart** (10). The **wrap** member provides a passive sustained dimensional **constraint** on a **heart** muscle. The **constraining** material is adjustable to **resist expansion** of the **heart** beyond one of the predetermined inner perimeters of the **wrap** member without **resistance** to **systolic** ejection.

USE - Used for **heart ventricle** to provide therapeutic **aid** to patients having **ventricular dialtation**.

ADVANTAGE - Enables **girdle** to be adjustable in size and **shape** over extended period of time to gradually decrease **ventricular dialtation**. Employs fluid filled passive **wrap** that provides for variable volume to be enclosed by **wrap**. Provides feedback system wherein sensors can be built into **indistensible** lining to measure its tension, thereby providing automatic feedback to hydraulic circuit controlling **wrap** volume. Employs tissue engineered lining to protect myocardium.

DESCRIPTION OF DRAWING(S) - The figure is the cross-sectional view of the passive **girdle**.

Heart (10)**Girdle** (17)

pp; 10 DwgNo 1/7

Derwent Class: P32

International Patent Class (Main): A61F-002/04

24/34/6 (Item 6 from file: 350)

DIALOG(R) File 350:Derwent WPIX

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012077694 **Image available**

WPI Acc No: 1998-494605/199842

Method of **treating** patient with **heart** having **ventricular dialtion** -
involves use of **girdle**, formed of material and structure that does not
expand away from **heart**, which is **wrapped** around **heart** muscle

Patent Assignee: ABIOMED R & D INC (ABIO-N)

Inventor: KUNG R T V; LEDERMAN D M

Number of Countries: 001 Number of Patents: 001

Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week
US 5800528	A	19980901	US 95490080	A	19950613	199842 B
			US 95581051	A	19951229	

Priority Applications (No Type Date): US 95581051 A 19951229; US 95490080 A
19950613

Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
US 5800528	A		9	A61F-002/04	CIP of application US 95490080

Abstract (Basic): US 5800528 A

The method for **treatment** of a patient, whose **heart** is characterized
by **ventricular dialtation** comprises the steps of, **wrapping** a **girdle**
around at least the **ventricle** of the patient's **heart**. The **girdle** is
wrapped such that it can adjust in size and **shape** to facilitate a
gradual reduction in the size of the **heart**. The method then involves
maintaining the **girdle** in a passive state for an extended period of
time. The **girdle** in the passive state conforms to the outer **shape** of
the **ventricle** and does not **expand** its dimension in a direction away
from the natural **heart**.

The **girdle** is formed of a sheet of material prestressed in the
plane of the sheet to a value below the elastic **limit** of the
material, the sheet having a tension which **limits** extension away from
the **heart** , while providing compression **forces** radially inward toward
the **heart** .

ADVANTAGE - Improves performance characteristics of the **heart**.

Dwg.1b,4/7

Derwent Class: P32

International Patent Class (Main): A61F-002/04